

# Correspondence

## Microprocessor-Assessed Adherence With Once- or Twice-a-Day Dosing With Sulfonylurea—No Difference

TO THE EDITOR: The frequency of daily dosing is a factor that is assumed to influence a patient's compliance with therapy. Research is sketchy, however, and was done on small groups.<sup>1</sup> Pharmaceutical manufacturers promote products based on perceived advantages in the frequency of dosing; formulary decisions often are influenced by this aspect of medications.

One of the most commonly cited studies that found a difference between once- and twice-a-day dosing was retrospective in design and had a study population of three patients on once-a-day dosing and six patients on twice-a-day dosing.<sup>2</sup> In a review of 57 articles on the relationship between patient adherence and dosing frequency, the rate of compliance with once-a-day dosing (73%) was similar to that of twice-a-day dosing (70%).<sup>3</sup> In this review, drug classes varied from study to study, as did the method of assessing adherence, resulting in methodologic limitation affecting the conclusions. Although there is no gold standard for assessing adherence, the recent availability of an electronic medication-event monitoring system (MEMS, Aprex) allows objective quantitative adherence data to be collected.

In two separate research protocols assessing sulfonylurea compliance in patients with diabetes mellitus, we used a MEMS. The aim of both studies was to compare objective adherence data from MEMS with those of alternative methods in patients with non-insulin-dependent diabetes mellitus. We pooled data from 70 men with a mean age of 68 years (range, 41 to 82). Mean compliance for taking sulfonylurea for all patients was 85.58%  $\pm$  19%. A total of 40 patients were on once-a-day dosing, with a mean compliance of 89.6%  $\pm$  13.5%; 30 patients on twice-a-day dosing had a mean compliance of 81.3%  $\pm$  23.3%. This was not statistically different from the once-a-day dosing, using a separate variance estimate *t* test.

The clinical importance of the difference in adherence between once- and twice-a-day dosing varies with the drug. Missed sulfonylurea dosing may result in decreased metabolic control and an increased risk for complications of diabetes. Twice-a-day dosing may be preferable in terms of therapeutic efficacy because the consequences of a missed dose may be milder than with a once-a-day regimen.

The similar adherence between once- and twice-a-day dosing for sulfonylurea suggests that adherence should not be a factor that influences prescribing when making a decision regarding once- or twice-a-day use of sulfonylureas.

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3. Greenberg RN: Overview of patient compliance with medication dosing: A literature review. *Clin Ther* 1984; 6:592-599

## Melanoma? Or Makeup?

TO THE EDITOR: In the Commentary in the July 1995 issue, Laurens P. White, MD, has taken up the question of a facial "lesion" in a well-known painting by Goya.<sup>1</sup> The painting is a group portrait of the royal family of Spain, done about 1800. White has concluded that the pigmented spot on the temple of the elder sister of King Carlos IV is a melanoma.

Gerald Hodge and I described Goya's depiction of the same subject and came to a different conclusion.<sup>2</sup> Large beauty marks were fashionable at the time Goya created this work. Goya also painted the king's wife, Queen Maria Luisa, with a similar "lesion" on her temple at least twice (see the exhibition catalogue that accompanied the Tokyo and Kyoto, Japan, Goya shows in 1971-1972, especially catalogue entries No. 5 and No. 27).

Is this pigmented "lesion" a melanoma, or is it makeup? Readers of THE WESTERN JOURNAL OF MEDICINE may wish to travel to Madrid to decide for themselves.

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2. Hodge GP, Ravin JG: Spanish art—A contribution to medicine. *JAMA* 1969; 207:1693-1696

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## Dr White Responds

TO THE EDITOR: Regarding the thoughtful letter of J. G. Ravin, MD, about Goya's painting, my commentary included an illustration of an area of the large group painting of the family of King Charles IV. Ravin thinks that the large, irregular black area on the right temple of the Infanta Maria Josefa was a "beauty mark." It was my contention that this area was surely a lentigo maligna, probably with a melanoma. In the article that Ravin wrote with his colleague, G. P. Hodge they showed the preparatory painting of the Infanta and concluded that the irregular black area on her right temple was cosmetic.<sup>1</sup> They stated that such large "beauty marks" were commonly used by Goya and others, and they illustrated this by showing other paintings.

I recently reexamined both the preparatory portrait and the finished group painting in the Prado in Madrid. The black area in question is irregular in outline and measures nearly 4.5 cm in longest diameter and just over